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THE MORPHOLOGY AND DEVELOPMENT OF INTESTINAL FOLDS AND VILLI IN VERTEBRATES

BY

WILLIAM A. HILTON, PH. D.

From the Histological Laboratory of Cornell University

WITH 2 TABLES AND 87 FIGURES

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THE MORPHOLOGY AND DEVELOPMENT OF INTESTINAL FOLDS AND VILLI IN VERTEBRATES.[1]

BY

WILLIAM A. HILTON,

From the Laboratory of Histology and Embryology, Cornell University.

WITH 2 TABLES AND 87 FIGURES.

For many years confused ideas have been prevalent concerning the form and occurrence of mucosal folds and villi in the different divisions of vertebrates, and even yet it is not entirely clear just where folds cease and villi begin. There are great variations in occurrence even in closely related forms, but much of this confusion may be due to the various methods of study which have been employed. Comparatively few investigators have made an extended study of the folds and villi in the different classes, although quite a number have made careful investigations of a single vertebrate class, and much work has been done upon the folds and villi of different species when the general digestive system of a typical form was described.

The phylogenetic study of an organ often reveals many perplexing structures which may render conclusions very doubtful. In such a study of folds and villi, difficulties present themselves which are almost insurmountable without the aid of embryology. So in order to obtain a correct idea of the primitive as well as the more advanced forms of mucosal elevations, it is necessary not only to make rather extended observations of numerous species of all great groups, but also to trace the development in several types of vertebrate embryos. The possibilities for work along these lines are very great, and in this investigation, only so far as time and material would allow, such work was attempted. An effort was made to determine as clearly as possible the limits of

[1] This paper was presented to the faculty of Cornell University as a thesis for the degree of Doctor of Philosophy, May 1902. I wish to express my grateful appreciation of the facilities placed at my disposal by the Department of Histology and Embryology, and for the aid and encouragement of the instructing staff. I am also greatly indebted to Prof. B. G. Wilder of the Department of Vertebrate Zoology, who very kindly enabled me to examine many valuable specimens which are in the possession of that Department.

folds and villi; to describe the character of folds and villi in some forms not already described as well as to supplement what was known about others; to determine, as far as possible, the form of folds and villi characteristic of different groups of vertebrates; to throw some light upon the development of villi in different forms—first, by the general survey of conditions existing in adult species; second, by embryological study of a few types.

Methods.

In order to obtain folds and villi in their usual form, fixation must be used which will not cause the muscular fibers of the *muscularis mucosæ* to contract and so produce unusual shapes. The intestines were usually injected and placed in the hardening fluids before the tissues had ceased to be irritable, so almost any of the fixing fluids which are rapid in their action were not desirable. Although formalin acts quickly, it was found to be very satisfactory, as the villi appear only slightly distorted, but it was not so useful when the finer structural elements were to be preserved. Müller's fluid, or a solution of 3 per cent dichromate of potash, does very well for preserving villi, in that the action of these fluids is slow and villi are seldom contracted; but when these fluids are employed, the epithelium is usually exfoliated. At times a rather high percentage of alcohol was efficient as a preservative, as the action was not rapid.

After hardening the intestines either in the fixing fluid or in alcohol, rather thick sections were cut in collodion; the thickness of the sections depending upon the size of the villi to be examined. Examinations of the whole intestine under liquids often helped to determine the character of folds or villi. When the muscular coats were thin enough, bits of intestine were stained with hydrochloric acid carmine, and mounted mucosa up. When this was not possible, villi were examined which had been isolated by scraping or cutting from the mucosa.

For counting and measuring folds and villi, various methods were used. The most satisfactory, but not always applicable, method was by means of an ocular micrometer in squares. When villi were very numerous and the walls of the intestine thick, they were counted by removing a measured bit of mucous membrane and isolating the villi from it, counting their tips or bases until by repeated trials, uniform results were obtained. In every case the intestines were studied by as many different methods as possible and the results compared.

The following is a list of the methods ordinarily used for each specimen:

1. Fixation by two or more methods.

2. Naked eye examination, with isolation of villi to be studied under a lens or microscope.

3. Cutting free-hand sections if possible.

4. Mounting mucosa up after staining, if the muscular walls were thin enough.

5. Cutting serial sections from tissues imbedded in paraffine or collodion.

For the work on embryological development of folds and villi the usual fixing and staining fluids were employed.

Character and Occurrence of Folds and Villi.

Mucosal elevations of the intestines may be considered under four heads: first, such as the typhlosole and spiral valve; second, valvulæ conniventes; third, simple more or less longitudinal mucosal folds; fourth, villi.

The first and second divisions hardly come under the scope of this discussion, but will be briefly considered.

It may be said that the typhlosole of lamprey is a simple or partially developed spiral valve. In Elasmobranchs, a high development of this organ is reached; here the spiral valves vary much in complexity, but are traceable directly or indirectly, with the help of embryology, to a simple type such as the typhlosole of lamprey. The Ganoidea apparently have more or less distinct remnants of spiral valves, while this peculiar type of intestinal folds is found to have reached a high development in the Dipnoi and Holocephali as well as the Elasmobranchii.

Ruckert, 96, described the development of the spiral valve of Pristiurus from spiral foldings of the mucosa; but it seems to me that the spiral valve is like a folding of the whole thickness of the intestine rather than of the mucosa and submucosa alone, and in the course of time the infoldings may have lost much of the original character of the infolded intestinal wall. I shall not attempt to explain just how or when this infolding took place, but it seems probable that it began before or with the formation of a simple spiral fold like the typhlosole. This infolding may be considered as similar to several coils of intestine which have come into very close contact; no essentially new structure is formed, simply a modified intestinal tube. The folding of the spiral is probably as much for retarding the progress of the food as for increased absorption area, because the absorbing area is not much greater than that of a coiled, small caliber intestinal tract; for where

the spiral valve is present, the intestine, although of considerable diameter, is very short. Hence, a very important difference, physiologically, may be noticed between the spiral valve and valvulæ conniventes, the first developed especially for retention or retardation of the food and greater compactness, and the second, formed especially for increased absorption area. The important difference already hinted at, is that spiral valves were formed from an infolding to a greater or less extent of the whole muscular walls as well as of the mucosa and submucosa, while valvulæ conniventes were formed by a simple fold of the mucosa and submucosa. This theory is partially based upon the following facts.

In the spiral valve of Lepidosteus and Amia, there is more muscular tissue than could have been derived from a double layer of the muscularis mucosæ.

There is a spiral fold in the cæcum of rabbits. When rabbits are born, this structure is not fully developed, its presence is marked on the exterior by constrictions, sections across these constrictions show the developing folds on the ental surface and the muscle of the muscular coats can be traced for some distance into the spiral core (Fig. 41). Of course this fold in the rabbit may not be homologous with the spiral valve of other forms, and the hypothesis outlined above requires much further investigation before it can be substantiated.

It seems that man is the only animal who can justly lay claim to *valvulæ conniventes*. It might naturally be supposed that some of the anthropoid apes would possess structures corresponding to some stage of these folds, however, careful examinations of specimens and a review of the literature on apes did not bring to light any clue to such structures.

The *valvulæ conniventes* of man begin their development shortly before birth and do not reach their full height until long after the villi are formed. They begin as small, transverse, semi-ringlike thickenings in the submucosa, these grow more prominent, those below the pylorus some distance become prominent more rapidly than others; as these thickenings project inward, they carry on their surfaces the villi of the mucosa (Fig. 42). The structure and arrangement of valvulæ conniventes in the adult are so well known as to require no redescription.

One particular more than another which may be worthy of note is the following: Brooks, 92, and Kazzander, 92, described valvulæ conniventes and both recognized in some cases, a spiral arrangement of the transverse foldings. Just what this signifies, it is difficult to

decide, but, to me, it seems doubtful that it indicates either a progress towards or a remnant of, a perfect spiral valve. If it indicates a developing spiral valve, it would probably develop in a different manner, as those of Elasmobranchs do. If a remnant of a once perfect spiral, why do we not see more forms between man and fish having this peculiar folding?

Simple, primary[2] folds of the mucosa are easily distinguished from secondary folds, such as the spiral valve and valvulæ conniventes. The simple folds are usually found when no villi are present, while the spiral valve or valvulæ conniventes may have folds or villi upon them. Then, too, the simple folds are more or less longitudinal in their distribution. They vary from thin or thick, slightly wavy to very wavy or zigzag forms, and sometimes they may have a net-like arrangement where some parts of the folds extend transversely. In no case do transverse folds entirely replace the longitudinal ones. It might seem from this that the original direction of the folds was longitudinal, but in the course of development, parts of the folds in some cases had come to take a transverse direction.

A villus is a projection of the intestinal mucous membrane covered with columnar epithelium and having its core made up of adenoid connective tissue; it also has a network of capillaries in this core supplied with one or more arterioles. In the central part of the villus and surrounded by the blood vessels, are one or more lacteals. Usually a villus has its base diameter much less than its height, but there are some exceptions to this. The distinction between a very broad villus and a small fold cannot be a sharp one; usually, folds are comparatively few and continuous, while villi are distinct and very numerous.

Villi are of many forms; they vary from thin plate-like kinds with square or rounded edges much like parts of folds, to long or short, slender or thick, cylindrical forms with rounded or sharp tips.

For convenience, the occurrence of folds and villi in different animals will be spoken of together. As other elevations of the mucosa have been discussed as far as it is necessary for the purpose of this paper they will simply be referred to occasionally. In many groups the conditions existing in different species have been carefully described by many investigators; besides giving a brief review of a few more important of the many forms studied by these, there will be added occasional supplementary descriptions and descriptions of forms hitherto undescribed.

[2] It seems best to consider as primary folds, those which are the simplest and the first to develop. The secondary folds develop later and independently.

Besides the typhlosole of Petromyzon, simple longitudinal folds are found in Cyclostomata; and the intestine of Myxine, according to J. Müller, 45, is entirely smooth except for a few very small longitudinal folds.

Villi have been described upon the spiral valves of Selachians by Pillet, 85. My own observations seemed to confirm this description.

In the intestines of Ganoids which I have been able to examine and from descriptions by various investigators it seems evident that net-like or zigzag, closely placed folds occur, but in Amia, the net-like fold arrangement is in many places broken up into free projections which are true villi (Hilton, 1900).

Many varieties of mucosal elevations occur in different forms of Teleosts. Villi have been described in *Orthagoriscus mola* by Rudolphi, 28, Owen, 68; *Esox lucius*, Grimm, 66. Meckel, 29, and Ratke, 37, have also described villi in a number of species. In the rather limited number of Teleosts I have been able to examine, no true villi were found, and in *Esox lucius* in which villi have been described, a simple network of true folds was found which might be taken for villi in sections, but could not otherwise be mistaken for them.

Three forms of folds were found in Teleosts:

1. The rather closely placed more or less wavy, thick folds; such as Macallum, 84, describes for *Amiurus catus* and those found in *Amiurus nebulosus* and *Perca flavescens* (Fig. 7).

2. Very low zigzag folds which are scarcely more prominent than those on the finger tips; such as those found in *Catostomus catostomus* one of the Catostomidæ (Figs. 5 and 10), or those of *Notropus cornutus* and *Phimephales notatus* of the Cyprinidæ.

3. Net arranged folds as those of *Esox lucius*.

There seems to be very little literature upon the mucosal elevations of Dipnoi and what little there is deals almost entirely with the spiral valve.

Leveschin, 70, described villi in *Salamandra maculata*, but in all American tailed Amphibia no villi were found. About the simplest condition was found in *Siren lacertina*, where the intestine in the specimens examined was smooth. The most common form of fold was a simple longitudinal rather straight or slightly wavy kind which in many cases was rather thick; such folds as are found in Necturus, Gyrinophilus, Amblystoma, etc. (Figs. 3 and 4). Another form of fold was found in the intestine of Amphiuma. In this animal the folds are quite numerous and zigzag with rather sharp angles (Fig. 2). Villi have been described in very few Anura. The folds described in Euro-

pean species and found in American forms are either somewhat net-formed, or much like those of Necturus, Amblystoma, etc., but may be larger and slightly more wavy.

Villi have been described by Langer, 86, in the genus Bufo; these villi are said to be long and overlap each other; but in *Bufo agua* Klein, 50, described net-formed folds. In *Bufo lentiginosus americanus*, I found a net arrangement of folds for a short distance beyond the pyloric valve. Isolated parts of these folds approximate villi (Fig. 9).

There are a few descriptions of villi in reptiles. Meckel, 17 and 19, has described villi in quite a number of forms and folds in some. Stannius, 46 and 56, described villi in crocodiles and in chamæleon. In the American representatives of this class which were available for study, no villi were seen and in the forms studied four different types of folds were found:

1. Long, plate-like, regular, parallel folds, which are rather thin, but usually quite high and thickly placed. Such folds are found in several species of turtles (Fig. 1).

2. Parallel wavy folds, similar to those of Necturus, etc., such as are found in some of the Colubridæ and Crotalidæ and some of the Lacertilia.

3. Very zigzag folds such as are found in *Bascon constrictor* (Fig. 8). In this species, the common blacksnake, besides these very zigzag folds, areas were found where the intestine either artificially or naturally, is of small diameter and at these places the zigzag folds are replaced by parallel flat longitudinal plates or folds.

4. Low, very zigzag elevations which differ from those of Cyprinidæ in being more prominent. In *Alligator mississippiensis* (Fig. 6) this type of fold was found.

The mucosal folds and villi of birds have received much attention from Owen, 67, Gadow, 69-79, Rudolphi, 80, and a number of others. The second of these authors quoted has done much more than any of the others and the following types of structures found in American forms correspond very closely to the structures given by Gadow for European species.

There are three of these divisions in which an attempt is made to show the occurrence of folds and villi in birds.

1. Folds and no villi.

(a) Zigzag folds, such as are found in some of the sparrows and described by Gadow in Monticola, Euphone, etc.

(b) Net-arranged folds, as in Murre (*Uria troile*); and in the genus Sturnus of Passeres described by Gadow.

2. Both folds and villi in the same intestine.

(a) With the folds net-formed. Gadow describes such a condition in the Allidæ. I was unable to find such a condition in any forms examined.

(b) With zigzag folds and usually their plate-like villi regularly arranged. Under this head come the mucosal elevations of *Nycticorax nycticorax*, night heron, Scoter duck or *Oidemia deglandi*, *Lars argentatus smithsonensis*, and a number of others. Gadow has described this condition for Oriolus, Lanius, etc.

3. Villi and no folds.

(a) Some of the villi in parallel rows, or otherwise regularly arranged.

In Flamingo, Owen, 69, described short villi in long parallel zigzag rows. Similar conditions are described by Gadow, 49, in Scolapax, Limosa and others. In a specimen of domestic duck some conditions were noticed which differ in several respects from any other form studied and so will be given in more detail.

Domestic duck.—In the upper part of the intestine of duck, the villi are quite regular and numerous. They are thin at first, square for the first part of their length, but near the tips, triangular shaped with sharp points. In many cases, two villi fit together; on one side the outer edge of one is thickened and each thick edge laps upon the thin edge of the other (Fig. 43). The villi are in quite close contact throughout their whole extent. This pointed sort of villus extends down the intestine for about 82 cm. and they are about 1.2 mm. high by .3 mm. broad at the base. There are about 12 villi to the sq. mm. For the last 63 cm. of the small intestine the villi become quite uniformly .6 mm. high by .3 mm. broad. They are thin, oblong plates with even edges and right angles. These villi are arranged very regularly and there are about 15 to the sq. mm. Upon looking down upon the surface of the intestine, it is seen that each side of the top of each one has presented to it the edge of the top of another villus (Fig. 44). In the cæca, the villi are somewhat smaller and elongated, .4 mm. by .15 mm. broad at the base (Fig. 45). In the large intestine, the villi are thin plates that have straight edges with right angles and are screen shaped. Each top looks like a broadened "v" when looking directly down upon it. These villi are about .6 mm. high by .8 mm. broad and are arranged in regular, parallel rows, the convexity of one villus fitting into the indentation of the other (Fig. 46). There are four or five of these to the sq. mm. In each cæcum there are about 7500 villi; in the large intestine about 16,000; in the small intestine, 440,000, or nearly 500,000 in all.

(b) With villi which are not regularly arranged. This condition exists in the intestine of ruffled grouse, or *Bonasa umbellus*, domestic turkey, chicken, humming bird (*Trochilus colubris*), red-eyed vireo (*Vireo olivaceus*) and many others. It has been described by Gadow for a number of forms including the genus Corvus of Passeres.

In the following table (page 468) particular attention is paid to the form, size and number of villi in several species of birds which were carefully studied.

It may be seen from the preceding descriptions and the table on next page that there are really only two distinct forms of villi with many slight variations. These are the thin leaf-like form and the tooth-shaped columnar form. It may also be observed that in birds villi or folds are found to a greater or less extent in the large intestine and cæca as well as in the small intestine.

The occurrence of folds in the intestines of adult mammals seems to be exceptional and villi are in most cases entirely confined to the small intestine.[3]

Cuvier, 10, Meckel, 26, Owen, 47, Leydig, 47, and others, have described ring-like somewhat spiral or oblique folds for Ornithorhynchus; these are most numerous near the pylorus and extend into the first half of the colon, leaving the caudal half smooth. Small "secondary" projections were described on these folds by Oppel, 97, but he was unable to state definitely the homology of either of these structures.

Folds have also been described in some of the Edentata, Cetacea and Sirenia, by Meckel, 19, Rapp, 37 and 43, Eschricht, 49, and several others; Leydig, 57, Forbes, 79, have described large folds in elephants.

Villi are usually described upon the folds in elephants. In a number of species of mammals where folds have been described no reference is made to the occurrence of villi. Unfortunately I was unable to examine any specimens of the mammals in which these folds have been described.

The forms of villi in mammals may be grouped under four heads:

1. Thin, leaf-like or plate-like villi.

(a) With square corners, as found in the intestine of musk-rat (Figs. 14-16).

(b) With rounded edges, as in the duodenum of man, the intestine of apes and monkeys and a number of rodents (Figs. 21-23, 25-27, and 34, 35, 37).

[3] Little mound-like elevations are present in the cæcum of rabbit. These are found to have central lacteal vessels and a capillary networks of blood vessels; and so may be spoken of as villi although somewhat reduced in size.

Bird.	Villi near the Pyloric valve small intestines.			Villi near the cæca small intestines.				Villi of the cæca.				Villi of the large intestines.				Total number of villi in the intestines.	Remarks.
	Form.	Size.	Number per sq. mm.	Form.	Size.	Number per sq. mm.	Number in small intestines.	Form.	Size.	Number per sq. mm.	Number in both cæca.	Form.	Size.	Number per sq. mm.	Number in large intestines.		
Domestic duck	Thin triangular with sharp tips.	1.2 mm. high by .3 mm. at the base.	12	Thin oblong plates with even edges.	.6 mm. high by .3 mm. at the base.	15	440,000	Somewhat tooth-shaped.	.4 mm. by .3 mm. at the base.	15	15,000	Thin screen shape.	.6 mm. high by .8 mm. broad	5	16,000	471,000	See figures 43–46 and intestinal curve No. 4.
Ruffed grouse..... (Bonasa umbellus).	Thin leaf-like.	1 mm. by .3 mm.	10	Somewhat tooth-shaped.	.6 mm. by 1.3 mm.	4	12,000	I—Villi near the small intestine somewhat columnar and pointed. II—Villi near the tip of cæca low, mound like.	I—.8 mm. by .2 mm. II—.3 mm. by .3 mm.	12-15	8,000	Large tooth-shape.	.6 mm. high by .3 mm. at the base.	6	4,000	24,000	In the last part of the cæca there are a number of rather high longitudinal folds upon, and between which numerous small wart-like villi may be seen. See intestinal curve No. I.
Bob-white ..... (Colinus virginianus).	Thin leaf-like.	.8 mm. by .3 mm.	8	Thin pointed.	.3 mm. by .3 mm.	12-15	7,000	I—Similar to above. II—Similar to above.	I—.3 mm. by .2 mm. II—.1 mm. high, .1 mm. broad	I—12 II—about 100	8,000	Tooth-shaped or somewhat finger-shaped.	.4 mm. high by .1 mm. at the base.	15	1,000	16,000	In the last part of the cæca there are a number of large folds upon and between which small wart-like villi may be seen. See intestinal curve, No. II.
Domestic turkey ..	Thin slender tipped	1.2-1.8 mm. by .4 mm.	12-15	Thin leaf-like.	.8 mm. by .2 to .3 mm.	15	990,000	Leaf-like.	1.3 mm. by .2-.3 mm.	15	66,000	I—Leaf-like in upper large intestine. II—3 cm. from anus, villi low wart-like.	I—.8mm. by .2-.3 mm. at base. II—.3 mm. by .3 mm.	I—15 II—3	54,000	1,110,000	Villi extend down the cæca about 8 cm. leaving the remaining half of each cæcum smooth.

Maryland yellow throat ..... Most of the villi are long slender .4 mm. high by .05–.08 mm at the base.
(Geothlypis trichas.)

Least flycatcher ..... Small almost columnar villi, .3–.4 mm. long by .08 at the base, about 200 per sq. mm.
(Compidonax minimus.)

Yellow warbler ..... Villi somewhat finger-shaped, .1 mm. by .05 mm. at the base. There are about 75–125 per sq. mm.
(Dendroica aestiva.)

Humming bird..... Villi are somewhat columnar but flattened and often sharp tipped. Near the pylorus they are about .6 mm. by .15 mm. broad at the base, and there are about
(Trochilus colubris.) 100 per sq. mm. Near the anus the villi are about .2 mm. by .035 mm. at the base and there are about 150 per sq. mm. In the whole intestine there are about 15,000 villi. (See intestinal curve, No. 3.)

Cedar bird ..... Zigzag folds closely placed, which in some places are broken up into villi .8–.2 mm. high.
(Ampelius garrulus.)

Scoter duck ..... Zigzag folds .8–.1 mm. high by .5–.8 mm. thick replaced in some places by isolated parts or villi.
(Oidemia deglandi.)

Night heron ..... Zigzag folds replaced in places by villi .8–.1 mm. high by .4–.7 mm. broad by .08–.1 mm. thick.
(Nycticorax nycticorax.)

Downy woodpecker ..... Near the pyloric valve villi quite broad, somewhat flattened and sharp pointed, 20–30 per sq. mm., 1 mm. high by .4 mm. at the base. Near the end of the
(Dryobates pubescens.) intestine villi are nearly columnar, .3 mm. long by .8 mm. wide at the base.

Great horned owl..... Near the pylorus villi about .8 mm. high by .15 mm. at the base and flattened columnar in form. Villi in rest of the intestine smaller. The villi continue
(Pubo. virginianus.) 4 cm. or half way into the cæca and the remaining 4 cm. of each cæca has no villi; but very low folds were formed.

Rough-legged hawk ..... The villi are almost perfect cylinders in some places, while in others they are somewhat flattened. The largest are about 1.5 mm. long. In the last part of

2. Very long cylindrical or thread-like forms such as are found in ox, opposum, camel and others (Figs. 11-13).

3. Short thick mound-like, or low columnar forms, such as are found in the cæcum of rabbit and the small intestine of horse, although this last very nearly comes under the next heading (Fig. 40).

4. Cylindrical villi, such as are found in cat, dog, raccoon, and some Insectivora and in the ileum of man (Figs. 17-19).

The following table (page 470) gives the results of observations on the form, size and number of villi in some of the mammals which were available for study.

In *Macacus cynomolgus* one of the primates, Rawitz, 94, describes small villi and larger "ramified" forms. In the intestine of a number of monkeys examined leaf-like villi were observed, and in specimens of Gorilla, Chimpanzee and Orang more or less leaf-like villi were found.

In the intestine of a child at term, the villi are thin, more or less leaf-like or fold-like. Many of these have broad bases and might almost be considered folds. Their height is from .2-.4 mm. by .2-.7 mm. at the base. The villi of a single region varied about as much as the villi of different regions differed from one another. Although the villi in one part of the intestine are very similar to those of other parts in height and general character, a slight difference can be noted, for the region near the pylorus has more fold-like villi than the central part. The central part has more long villi of a triangular shape than has the upper part of the intestine, and near the end of the small intestine there are more villi with their tops nearly as broad as their bases. There are from 10-12 villi per square mm., and in the whole intestine, about 1,000,000 (Figs. 25-28) and (Intestinal curve No. 12).

In adult man, Stöhr describes leaf-shaped villi in the duodenum and cylindrical in the rest of the intestine. Sappey estimates the number of villi in man to be from 6,000,000 to 10,000,000. Others estimate 4,000,000. The greater number of villi in the adult are in the upper part of the intestine, 10-18 per square mm.; farther towards the cæcum, 8-14 per square mm. Many authors have described club-shaped villi in the intestine of man, but when thin sections are made of cylindrical villi which were fixed in some such fluid as picric acid, club-shaped forms are found; so it seems improbable that club-shaped villi in man are typical.

Intestinal Curves of Mammals and Birds.

In the following diagrams (p. 471) the relative height of villi is indicated by the distance of the continuous curved lines above the heavy

Animal.	Villi of the small intestine near the pyloric valve.			Villi of the small intestine near the center of the intestine.			Villi of the small intestine just above the cæcum.			Total.	Remarks.
	Form.	Size.	Number per sq. mm.	Form.	Size.	Number per sq. mm.	Form.	Size.	Number per sq. mm.	Number of villi in intestine.	
Calf a few days after birth	Thread-like slender cylinders.	.5–.8 mm. long by .1 mm. at base.	18-20	Thread-like.	.4–.6 mm. long by .15 mm. at base.	25	Thread-like.	1 mm. long by .1 mm. at base.	25	20,000,000	See Figs. 11–13, Pl. II.
Domestic rabbit	Thin leaf-like rounded tips.	.5 mm. by .9 mm.	5-6	Thin leaf-like triangular shaped.	.5–.7mm. by .2–.3 mm.	1	Almost thread-like but rather broad base than tips pointed.	.6 mm. by .1 mm.	30	900,000	In the cæcum there are numerous small mound-like villi. In the small intestine nearest the pylorus there are numerous short folds or fold-like villi .15 mm. high by .8 mm. long. (See Figs. 20–24, Pl. II.)
Mouse (Mus musculus).	Thin leaf-like rounded tips.	.5 mm. by .3 mm.	20	Thin leaf-like triangular shaped.	.35 mm. by .15 mm.	40	Thin points almost cylindric; slender.	.1 mm. by .03 mm.	40	130,000	See Figs. 34–39, Pl. II, and intestinal curve, No. 9.
Muskrat (Fiber zibethicus).	Oblong, thin, flat with sq. ends.	1.4 mm. by .4 mm.	10	Oblong, thin, flat with sq. ends or nearly so.	.8 mm. by .3 mm.	10-12	Oblong thin flat plates.	.4 mm. by .2 to .3 mm.	10	500,000	See Figs. 14–16, Pl. II, and intestinal curve No. 8.
Grey squirrel (Sciurus Carolinensis).	Thin leaf-like.	.3 mm. by .4 mm.	5-8	Thin leaf-like triangular shaped.	.2 mm. by .1 mm.	20	Thin, slender, pointed.	.5 mm. by .1 mm.	30	Not determined.	
Porcupine (Erethizon dorsalis).	Thin leaf-like without rounded edges.	1.4 mm. by .6 mm.	5-7	Thin leaf-like triangular.	.3 mm. by .3 mm.	10-12	Thin, slender, pointed.	1 mm. by .3 mm.	12-14	20,000	Near the pyloric valve there are a number of little folds with wavy edges. (See intestinal curve No. 11.) The greatest extent of one of these is 3 mm.; besides these small wavy folds which look much like villi pointed at their bases, there are few rather low thin straight folds 5-10 mm. long, .1 mm. thick and 1 mm. high.
Adult domestic cat (From several specimens).	Cylindric.	.5 to .7 mm. high by .1 mm. at the base.	15	Cylindric.	.3 mm. high .2 mm. at the base.	20	Cylindric.	.5 mm. h. by .06 mm. at the base.	25	1,000,000	See intestinal curves Nos. 5 and 6 and Figs. 17–19, Pl. II.
Half grown cat	Cylindric.	.5 mm. by .08–.1 mm.	15	Cylindric.	1.8 mm. by .15–.18 mm.	20	Cylindric.	.3 to .5 mm. by .06 mm.	25	600,000	The smaller number of villi in this animal is largely due to the smaller size and length of the intestine than that of an adult cat.
Adult domestic dog	Cylindric.	.8 mm. by .2 mm.	12–15	Cylindric.	.3 mm. by .25 mm.	15–20	Cylindric.	.7 mm. by .15 mm.	20–25	2,000,000	
Domestic dog a few days old	Cylindric.	.6 mm. by .1 mm.	15	Cylindric.	1.2 mm. by .2 mm.	20	Cylindric.	.4 mm. by .1 mm.	25		Throughout the small intestine there was a great number of much smaller villi; .2 mm. high by .05 mm. thick; these small villi are probably the beginnings of new villi which are formed since birth.
Raccoon (adult) (Procyon lotor).	Cylindric.	.4 mm. by .1 mm.	10–12	Cylindric.	.8 mm. by .12 mm.	10–12	Cylindric.	.3 mm. by .05–1 mm.	15–20	190,000	As there is no cæcum the villi described under the last three columns are from near where the villi end or 25 cm. from the anus.
Raccoon (half grown). (Procyon lotor).	Cylindric.	.3 mm. by .1 mm.	20–25	Cylindric.	.4 mm. by .1 mm.	30	Cylindric.	.1–.2 mm. by .05–.08 mm.	40	125,000	Villi described under the last three columns are from where the villi end or 16 cm. from the anus.
Opossum (Didelphys virginiana)	Thread-like slender cylinders.	3 mm. by .1 mm.	5-6	Thread-like slender cylinders.			Thread-like slender cylinders.				Near the cæcum the villi are smaller but much like those of the pyloric region in shape.
Shrew-mole (Blarina brevicauda)	Cylindric.	.5 mm. by .1 mm.	50-80	Cylindric.	.3 mm. high by .06 mm. thick	80	Cylindric.	.2 mm. by .04 mm.	80	180,000	The last three columns are where the villi end or 3 cm. from the anus. (See Figs. 32 and 33, Pl. II.)

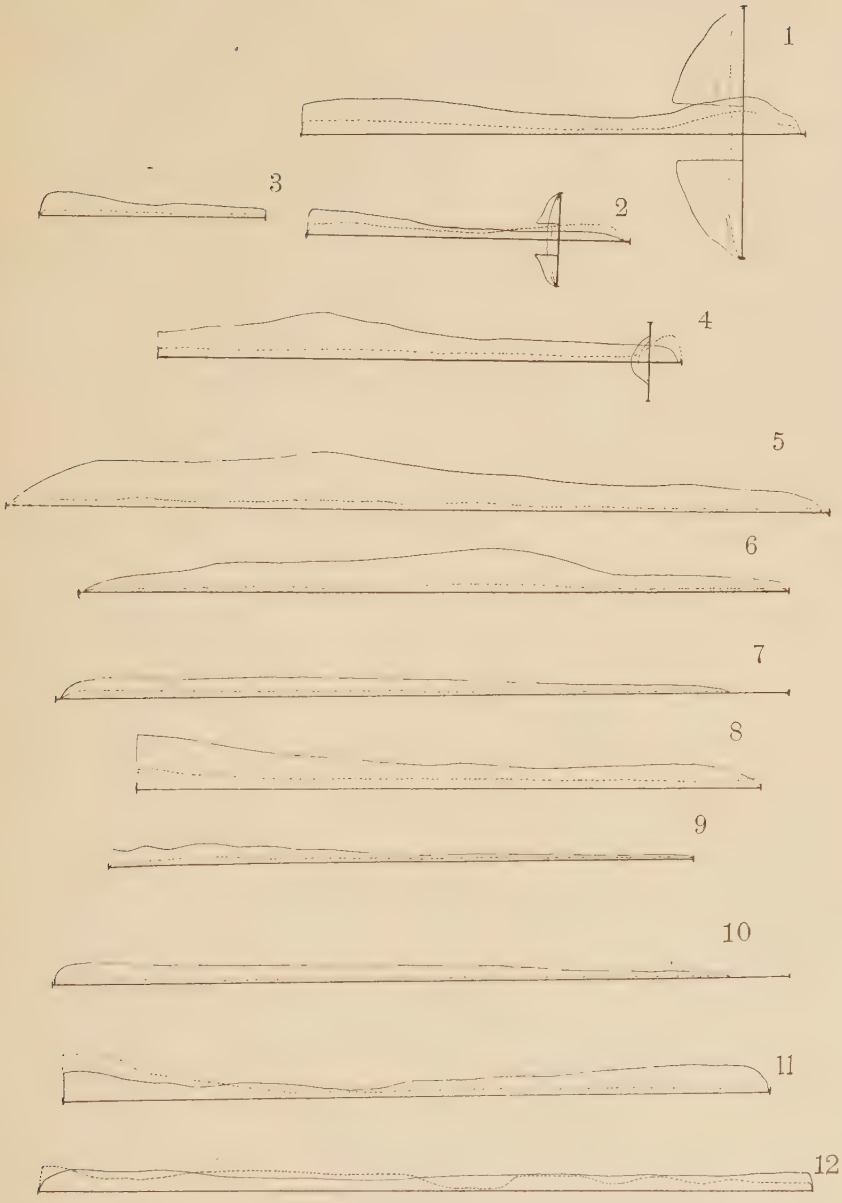

Fig. 1. Ruffled grouse
Fig. 2. Bob-white
Fig. 3. Humming bird
Fig. 4. Domestic duck
Fig. 5. Old cat
Fig. 6. Young cat
Fig. 7. Bat
Fig. 8. Muskrat
Fig. 9. Mouse
Fig. 10. Shrew mole
Fig. 11. Porcupine
Fig. 12. Homo at term

base line and the relative breadth of villi by the distance of the dotted lines from the base line. The left hand of each diagram represents the cephalic, and the right the caudal end of the intestine.

In Figs. 1, 2 and 4 of birds, the cæca are indicated by the heavy perpendiculars above and below the base line. All of the base line to the right of these perpendiculars indicates the small intestine.

In Figs. 1 and 2 large folds in the cæca are indicated by the curved lines which are the farthest from the base line.

THE DEVELOPMENT OF FOLDS AND VILLI.

The development of folds and villi may be considered in two ways:

1st, by the study of the different stages found in adult species.

2nd, by the study of their embryological development in one or more animals.

By a brief review of the typical forms found in some intestines described, it may be seen that in a simple type of intestine only slight longitudinal folds occur. In some other species there are rather more prominent, nearly straight folds; in others, wavy folds are found, and in some others very wavy or zigzag folds may be seen. In a few species, net-arranged folds are observed.

The investigations of recent years and the researches described in the present paper, point unmistakably to the conclusion that both phylogenetically and ontogenetically villi are developed from mucosal folds. The phylogenetic development may be illustrated in two ways by various groups and may be made out quite well in animals where folds and villi occur in the same intestine.

The simplest way in which villi are developed from folds is their formation from long, very zigzag, longitudinal ones, such as described in the blacksnake, sea gull, night heron, cedar bird, etc. Villi seem to be formed by simple separations at the angles of the folds. In several forms of animals, such as the wild duck or the night heron, zigzag continuous folds are found on one part of the intestine and in other places the villi are arranged in zigzag rows; these rows look like folds but are broken up into villi. In some intestines, such as those of the chicken or the turkey, villi are found which are not regularly arranged and no folds occur in the adult.

Another less common method of development of villi is the development from the net-formed folds. In this method probably very zigzag folds unite with each other, making a rather even network; later in

development this network becomes broken up into a more uneven arrangement by growth of the intestine, and the connections of meshes come to be separated; so here and there villi begin to be isolated from the folds and possibly, also, by farther unequal growth, villi come to entirely replace the folds. This method, although undoubtedly occurring in some forms, as in Amia where all grades of such development are shown, is probably not so common as the development from zigzag folds. In birds, for instance, it seems to be rather rare. Development, as shown by embryology, is very necessary to confirm the rather scattered results of the study of adult conditions.

Development of Villi in the Chick.

Plates III, IV and V, Figures 47-58 and 60-70.

There is a great variation noticeable in the intestines of chick embryos; even those of the same size and same age may differ much in regard to the development of the mucosa. In the following discussion the time of incubation is taken as a criterion of age and only those embryos are described which seem to show typical stages of development.

In some early embryos different stages of development may be found in different portions of a single intestine, therefore it might seem possible to obtain all stages from one intestine, but this is only true to a certain extent; so specimens of different ages are necessary in order to determine exactly what takes place in all parts of the intestine.

All parts of a seven day chick's intestine appear without folds or other elevations of the mucosa.

At eight days' incubation, rather large longitudinal folds of the mucosa make their appearance in the pyloric part of the small intestine. A cross section of the intestine at this place usually shows about three large folds (Fig. 48). These folds continue for some distance (Figs. 60, 61), but as the caudal portion of the intestine is approached they decrease in size and number and the last of the intestine shows no folds (Fig. 47); or the typical condition of earlier embryos.

In the small intestine of a nine-day chick there are seen to be six to seven folds which are somewhat smaller than those of the eight-day chick. They are also much more distinct. These folds are parallel, longitudinal and nearly straight (Fig. 49, A and B, and Fig. 62). Towards the cæcum these folds are less numerous and in the last part of the small intestine they are entirely absent.

In the duodenum of a ten-day chick, there are from 9-16 longitudinal folds which vary somewhat in size. Some are low and rather shorter than others. Most of the folds near the pylorus are rather wavy from side to side, but some are nearly straight. Farther along in the small intestine the folds are less numerous or entirely absent.

In the small intestine of an eleven-day chick the longitudinal folds near the pylorus have become quite wavy from side to side (Fig. 50 A and B, and Figs. 63-64). Farther towards the cæca they are less numerous and not so wavy; still farther along there are only about ten straight folds; and next the cæca there are a few folds or mound-like elevations, shorter and thicker than the others.

In the small intestine of a thirteen-day chick the folds are found to be very zigzag, the angles made by the folds are quite sharp; the tops of these folds are more or less divided, that is, partially broken up into villi (Figs. 51, 52). Lower in the intestine, similar folds are observed for some distance, or in places irregular elevations of epithelium which are possibly short folds. Towards the cæca the folds nearly disappear.

In a chick of fourteen days almost perfectly formed villi are found in the duodenum (Fig. 53). In sagittal section these villi are seen to be united at their bases, so they form zigzag folds, partly divided into villi at the free edges (Fig. 54). Villi have been formed in part by folds becoming very zigzag, the epithelium of the sharp fold angles is in this way gradually brought in contact and then separation into villi takes place from the tips downward (Figs. 69 and 70).

Lower in the small intestine less advanced conditions of folds are found, but just above the cæca the conditions noticed cephalad are much less evident and it is very probable that villi are formed here, without going through all the fold stages.

In a fifteen-day chick there was found a remnant of the zigzag arrangement of villi; short folds were noticed similar to the larger ones of earlier embryos.

In the small intestine of a sixteen-day chick there are true villi and the zigzag arrangement is absent throughout.

Up to about ten days of incubation there are no folds in the cæca, but at ten days a few rather large irregular folds appear. At eleven days a few large thick elevations may be seen, but most of each cæcum is bare of folds of any sort. At thirteen days the cæca have thick irregular mounds (Figs. 55 and 67). These elevations grow upward irregularly so that some parts outstrip others; as growth proceeds, the elevations become divided into smaller and higher projections and at fourteen days these may be spoken of as low villi of various sizes,

thickly placed and irregularly distributed (Figs. 56 and 66). The further growth and multiplication of villi in the cæca was found to be the same as in other parts of the intestine. The development of villi in the large intestine does not begin until eleven or twelve days of incubation, then small folds occur in some places, these may go on growing and help to form villi in the way in which they are formed in the cæca, but later stages show very little signs of villi formed as they are in the cæca. Thirteen- or fourteen-day chicks show quite uniformly throughout the large intestine, very small elevations which begin at first as simple elevations of epithelium, later a connective-tissue core seems to push up into these little elevations and true villi are formed by further growth (Figs. 58 and 65).

The development of villi in chick may be summarized as follows:

At first the intestine is entirely free from elevations of any sort. Later, rather large parallel folds of the mucosa gradually make their appearance in the small intestine; first near the pylorus. These folds soon become more numerous, the large folds divide into smaller ones and rather small new folds are developed between those originally formed; and in some cases these later folds also pass through all the stages which the earlier ones do. The slightly wavy folds become more wavy, first in the pyloric part of the intestine, and later more caudad; this wavy appearance becomes more and more marked until those which are at first slightly zigzag grow very zigzag. The angles become very acute and epithelial cells from both sides of many of these begin to nearly touch each other in the centre of the folds. This last is especially true of the tips of the folds. Villi are later formed by unequal growth and separations at the sharp fold angles from the tips downward. This separation begins when the folds are first very zigzag; the complete separation into villi occurs quite late in some parts of the small intestine, and long after the first folds are developed, villi make their appearance between other villi, without passing through a fold stage. In the lower part of the small intestine, many of the stages noticed in the upper intestine are entirely omitted and villi are developed, either from short irregular elevations, or as simple upgrowths of the mucosa.

After all traces of folds are lost the villi grow very rapidly in height and new villi are formed as simple upgrowths of the mucosa. Villi in the cæca do not make their appearance until some time after their beginnings are formed in the small intestine. They are formed from thick irregular elevations or short mucosal folds which gradually become divided into smaller but higher projections by their own unequal growth.

In most cases the large intestine remains without villi for a longer period than the cæca; here the thick irregular elevations similar to those in the cæca are seldom found. In the large intestine numerous very small processes composed entirely of epithelial cells make their appearance, connective-tissue cores penetrate into these projections and in this way villi are formed without passing through a fold stage. Later villi develop as simple upgrowths of the mucosa, probably without being preceded by the small, purely epithelial processes.

The Development of Villi in Mammals.

Plate VI and Fig. 59.

The development of villi in mammals has been recently studied by Voigt, 99, and Berry, 1900. Voigt speaks of villi formed in pig from large elevations of the mucosa which gradually become broken up by means of depressions; from these elevations villi grow up. Berry describes a similar method of villus formation in man, but he shows a little more clearly that the first elevations of the mucosa are in the form of rather large, irregular, longitudinal folds; these folds become broken up into villi.

The following presentation of the development of villi in mammals is confined to the intestine of the white rat.

As no idea could be obtained in regard to the age of the embryos, size alone is given, although this often expresses very little about the stage of the embryo's development.

Nowhere near the amount of material was available as in the study of chick, but in a way it was not required because the development of the villi is more direct and uniform than in chick.

The first indications of folds in the intestine of the white rat was seen in embryos of about 16-20 mm. from the base of the tail to the tip of the snout. The first folds are usually made up of very thick epithelial masses, these are somewhat short and generally run parallel, with the lumen of the intestine (Fig. 75). Into some of these very early folds a developing core of connective tissue may be seen. In an embryo of 33 mm. there were several large, thick, rather regular and parallel folds with well-marked connective-tissue cores; there were four near the pylorus which nearly filled the lumen (Figs. 76 and 77), two were large and two smaller, but after extending parallel for about 1.5 mm. there were only three folds and 1 mm. farther caudad only two folds and soon these ended (Figs. 71 and 72).

No wavy or zigzag folds were found in any of the specimens but in every case, villi either developed from parallel or irregular folds (Figs. 73, 74 and 79-80), or arose entirely without folds.

An embryo of 34 mm. which was much more advanced than the one of 33 mm., showed the lower parts of the intestine more or less free from folds, but in most of the intestine various stages of folds were found partly broken up into villi (Fig. 73). In some cases villi appear to be formed without passing through a fold stage, but usually, as in different parts of the intestine of this embryo, villi were formed from folds, that is, these folds grew higher and became divided into smaller but higher portions by irregular and unequal growth, and these projections soon grew like the villi of the adult.

The large intestine of the white rat is rather backward in its development, villi are not formed until the embryo is 40-50 mm. in length and then as in chick, the villi first appear as solid epithelial processes into which later the connective-tissue cores extend. Such a development of villi has been described in the large intestine by Brand, 77, and Patzelt, 82.

In the white rat the development of villi may be summarized as follows:

Folds are first formed near the pylorus; they are rather large, regular and parallel. Similar folds develop later in other parts of the intestine, but in some places no folds are formed. By unequal growths the folds gradually break up into villi and new villi are also developed without passing through a fold stage (Fig. 57). The beginnings of villi in the large intestine may be first recognized as little elevations of epithelial cells (Fig. 59). A core of connective tissue pushes up into these cell masses and the villi grow upward and become like those in other parts of the intestine.

The development of villi seems to take place rather early as compared with chick and the zigzag fold stage so characteristic of birds is lacking.

Disappearance of Villi from the Large Intestines of Mammals.

(Figures 81-87.)

It is well known that villi occur uniformly in the small intestine alone in adult mammals, but there are a few exceptions. In the cæcum of adult rabbits there are a number of very low mounds which are

found to contain a central lacteal surrounded by the usual villus network of blood vessels. These little elevations resemble the villi of the duodenum more closely than any of the other villi of rabbit and they are without doubt true villi, although much reduced in size. In some animals, such as raccoon, where no cæcum is present, only the lower part of the intestine is free from villi.

Excluding the forms mentioned above, mammals may be said to have no villi in the cæcum or large intestine of the adult.

Villi are usually present in birds and in the majority of forms where they occur they are found throughout the small and large intestine including the cæca, although in some cases the lower large intestine and tips of the cæca present variations in this respect.

Although villi do not occur in the large intestines of adult mammals, they do occur in the intestines of advanced embryos;[4] and in some cases where the young are born in a very immature condition, villi persist for some time after birth. The mammals in which villi are found in the large intestine for a short time after birth, have not been determined to any extent, but at least two forms in which this is the case are rabbit and white rat. Examples of intestines where villi disappear before birth are those of man and cat.

In a consideration of the way in which villi disappear in the large intestine of mammals, the following will be confined to their disappearance in the white rat. In this form they persist for a considerable time after the rats are born, and are not entirely absent from the large intestine until 12-14 days after birth.

Before starting with the discussion of the manner in which villi disappear, it will be necessary to speak of the development of the crypts of Lieberkühn, for it has been assumed that there is an intimate relation between the development of the crypts of Lieberkühn and the disappearance of villi.

Lieberkühnen crypts occur in the adult scattered irregularly in the small intestine. They are especially numerous in the ileum, but in the large intestine including the cæcum, they are so numerous that their mouths take up a large part of the intestinal surface. These crypts are simple or occasionally two-branched tubes or follicles of epithelium extending down into mucosa and usually nearly reaching to the muscular coats of the intestine.

[4] An interesting point in regard to the intestine of man which has apparently hitherto escaped observation is the fact that villi are found at one time in the vermiform appendix.

These glands of Lieberkühn were first described by Malpighi in 1688 and later by Lieberkühn in 1745.

The occurrence of these structures in fishes is doubtful, in Amphibia and Reptiles there are small areas where new epithelium is formed, or in other words, centres of cell generation; these little areas may be homologized with the crypts of higher forms. In birds there are crypts which are similar to those of mammals in all respects except size.

As to the manner of their development there have been many different interpretations by the investigators who have given them attention. Voigt, 99, summarizes the work which has been done on the development of these crypts, so a short review is all that is necessary to repeat before beginning the description of the crypts in the white rat.

Kölliker, 61, describes Lieberkühnen crypts in the beginning as deep out-growths of the epithelium, that is, down-growths.

Barth, 68, thought that the glands did not arise as down-growths (Ausstülpungen) of the epithelium, but that under the epithelium was a mesodermal layer from which villi and glands were developed. In the large intestine a similar development was said to take place.

Brand, 77, arrives at the following results: In the large intestine between the papillæ which develop from the surface, the glands are slowly formed. In the small intestine the villi are thickened at the bases, these touch and unite with each other and so separate walls appear, so the tube-like hollow Lieberkühnen glands are formed.

Kölliker comes to express similar views in his text-books of 79 and 94, and later editions of his works give the development much as the following.

O. Schultze, 97. In the stomach and large intestine, papillæ or villi are described which unite by means of low folds, so that little dimples appear, from each of these a deep insinking or end of a gland appears. Later these connecting folds or borders reach to one-half the height of the villi; so now the surface of the intestine appears as a honeycomb. At last the binding folds reach the top of the villi and at their disappearance the whole mucous membrane has the appearance of a honeycomb, in the mucosa are numerous glands which completely fill up the space.

In the small intestine there is a similar formation except that in the depths between the villi, the surface of the mucosa furnishes net-formed, binding folds and the epithelium from the so arising depressions push in short hollow sprouts. The gland formation is not so striking here because the villi during the formation of glands do not dwindle, but on the contrary, become longer.

Whether these depressions and epithelial processes further develop together or whether the epithelial tube later develops in the depths, remains undecided, but it is probable that earlier or later these epithelial tubes develop in the depths.

Patzelt, 82, studied the large intestine; he recognized small elevations of high epithelial cells, the anlages of later villi. Between these, in groups, short broad epithelial cells with basal nuclei, the anlages of the Lieberkühnen crypts, so that these lie in small depressions between them. Later between the villi, connective-tissue folds are elevated, the villi are in this way bound together so the crypts of Lieberkühn are formed by elevations of the wall, not at all or but slightly by deep growths.

Minot, 92, describes the Lieberkühnen glands as hollow outgrowths of entoderm extending into mesoderm. Kollmann, 98, describes the crypts of Lieberkühn as developed between the villi, making insinkings into the depths of the mucosa.

Voigt, 99, has studied the intestine of pig and comes to results contrary to those of Brand and Patzelt. He describes the intestine at first smooth, then furrows appear which divide the mucous membrane up into more or less isolated elevations and from these elevations villi grow upward, while from the furrows which form a network of connected canals, the crypts of Lieberkühn grow downward as hollow sprouts. Any development of the villus base to form the crypts of Lieberkühn, as seems possible, does not take place.

The intestine of the white rat is in some respects rather unfavorable for the study of the crypts of Lieberkühn, although it is more favorable for the study of the disappearance of villi.

An embryo of 43 mm. in length has crypts in the lower large intestine while no crypts were made out in the small intestine, although the villi were well formed. About the time of birth crypts begin to make their appearance in the small intestine and beginnings may be made out as little areas which appear like slight thickenings or depressions of epithelium, scattered irregularly over the surface of the intestine (Fig. 81). It often happens that one of these crypts begins near a villus base, but this seems to be purely fortuitous (Fig. 83). From birth onward the crypts become more numerous, as do the villi, the latter grow up as little buds of epithelial cells (Fig. 57). The crypts, on the other hand, begin as slight thickenings or slight depressions which vary somewhat in character, but are not sharp depressions at first; later they become more marked and after about five days are like little flasks with narrow necks and small lumens (Figs. 83-86). This character they keep

for some time, later they grow downward and at about three weeks after birth they have the characteristic appearance of long, narrow crypts and appear like continuations of the bases of the villi in the submucosa (Fig. 87).

The development of the crypts in the large intestine is much more clearly seen in some cases, because as development proceeds fewer new villi are formed than is the case in the small intestine. The development of the crypts in the large intestine was found to be similar to those farther cephalad, but apparently we have a sort of compensatory development as follows: In the small intestine few glands are developed between the primordial villi, but as the intestine proceeds with development new villi (such as Fig. 57) are developed between the already formed villi and glands, but in the large intestine after the first villi are developed, there are very few formed from buds, as in the case of the small intestine, and to take the place of such a formation many more crypts are developed than is the case in the small intestine.

So far as my observations go all these intestinal glands develop by a downgrowth of the epithelial surface, similar to that described by Kollmann, 98, and Voigt, 99.

In some cases a crypt may be seen to start at the edge of a villus base, but careful study has convinced me that without doubt the apparent relation of villus and crypt is only apparent, and one may see that in order to have glands composed of bases of villi, it would be necessary to have villi on all sides of a crypt, which is clearly not the case; not only do villi occur which are not near any crypts, but crypts occur which are not near any villi, as can be seen upon looking down upon a bit of mucous membrane from the intestine of a young animal in which some crypts may be easily recognized as well as some others which are just making their appearance (Fig. 81). Such a view shows the young and older crypts very small as compared with the villi and they appear as little circular dark-staining areas scattered irregularly over the mucous membrane. Comparatively few at an early stage are near villi; later as more glands and villi develop it more often happens that we find villi and glands very near each other.

In early stages Patzelt and Voigt recognized the anlages of the Lieberkühnen crypts as little thickened areas of cells between the villi; these areas take a deeper stain and so may be recognized. In white rat these are difficult to observe because they do not stain much more deeply than other parts of the epithelium, but after careful observation these beginning crypts may be recognized first by slight thickenings, then depressions, which take a little darker stain in some cases, due

to the crowding together of a number of nuclei. In later stages the crypts are more easily recognized and they often take a deeper stain than other parts of the epithelium, and because they extend deeper into the submucosa than the simple spaces between villi. This last distinction of course only becomes evident as glands have passed their earliest stage (Fig. 83).

The white rat is better adapted for a study of the disappearance of villi from the large intestine than many other mammals because in this form the villi persist some time after birth, twelve days or more, and so may be studied in all stages.

Villi begin their disappearance early. Just before birth the lower large intestine is entirely free from villi and glands occupy nearly all the surface of the rectum.

In white rat, villi are formed first, then glands are developed in the surfaces between villi and then later, villi disappear in the large intestine. This order of development seems to be quite constant and at first sight it appears as though the disappearance of the villi is in some way associated with the development of glands. There is very little literature upon this point. Minot, 92, states the general view as follows: "Villi also appear throughout the large intestine, but are obliterated there by an upward growth of glands."

As will be remembered Brand and Patzelt believed in the development of glands by means of an upward growth not a downgrowth, and the idea of Schultze and Minot that glands are in part formed by villi, places their opinion midway between the upgrowth and downgrowth theories of gland development; but so far as the disappearance of villi is concerned the upgrowth theories and the views of Schultze and Minot may be said to agree quite closely. Scherman in 98, studied the degeneration of the villi in the large intestine of guinea-pig and found that the upper four-fifths of the villi were composed entirely of epithelial cells; only the basal fifth was found to contain a core of connective tissue. When the villi begin to disappear by disruption, only this basal part persists and passes into the formation of Lieberkühnen glands. He states that in other mammals there is no real degeneration or disruption although the villi are used in forming the glands.

Voigt, 99, did not determine how villi disappeared from the large intestine, but found no disruption and no evidence to indicate that villi had anything to do with the formation of crypts. He considered the possible disappearance of villi by means of growth of the intestine, but did not bring forward any proof of this possibility.

A few facts which seem to point to an intimate relation between the disappearance of villi and the growth of the intestine may be given.

In white rat, very few new villi are formed after birth by buds of epithelium in the large intestine, the large intestine and cæcum at first grow very rapidly in length and diameter, but hardly at all in thickness of the intestinal wall, and during this rapid growth villi grow smaller and smaller until finally they disappear (Fig. 82).

The following measurements are given to show the rapidity of growth.

White rat of 5 days. (Length 6.6 cm.) Large intestine 3.3 cm.; cæcum, .5 cm. Villi in cæcum and upper large intestine.

White rat of 7 days. Large intestine, 4 cm.; cæcum, .7 cm. Villi in cæcum *going* but numerous in upper large intestine.

White rat of 8 days. Large intestine, 4.2 cm.; cæcum, .8 cm. Villi in cæcum nearly gone. Villi in the upper large intestine beginning to go.

White rat of 9 days. (Length 7.8 cm.) Large intestine, 4.9 cm.; cæcum, 1 cm. No villi in the cæcum but few in the upper large intestine.

White rat of 10 days. (Length, 7.3 cm.) Large intestine, 4.7 cm.; cæcum, .9 cm. A very few villi in some places of cæcum and a few in the upper large intestine.

White rat of 11 days. (Length, 8.5 cm.) Large intestine, 5 cm.; cæcum, 1 cm. No villi except a very few small ones in the upper large intestine near the folds.

As to the decrease in height of villi, the following is given for the cæcum, a similar decrease takes place in the large intestine.

5 days, longest villus .3 mm. high.
6 days, longest villus .2 mm. high.
7 days, longest villus .08 mm. high.
10 days, longest villus .035 mm. high.

If the glands were formed by part of the villi we might expect the crypts to be much longer after the villi had been obliterated, but as a matter of fact the crypts are not in the least longer just after the villi have disappeared.

The cæcum is a rapidly growing part of the intestine and villi disappear here after they have ceased to exist in the lower large intestine; that part of the large intestine which retains its villi until the last is the large intestine just below the cæcum, here as already shown the villi persist for a long time after they have disappeared elsewhere. In this region in the adult there are numerous nearly longitudinal folds which

run slantingly about the lumen. These folds of mucosa begin some time before birth and grow larger until in the adult they are of considerable size. They are at first largely made up of epithelium with four or more irregular layers of nuclei. These epithelial folds at first contain a small core of connective tissue, but this soon grows larger and the epithelium becomes similar to that of the adult. Glands grow into the core of these folds until in the adult these folds are almost solid masses of glands. These folds radiate from the junction of the cæcum and colon and from one or more thickened centres of intestinal mucous membrane. They are without doubt homologous with the papillæ filled with Lieberkühnen crypts which occur in a similar location in the rabbit's intestine. As to the bearing these folds have upon the disappearance of villi, it seems probable that the growth of these folds inward must have kept the mucous membrane of this region in a more folded condition than elsewhere, and it may be that villi were not so quickly drawn out as in other places. As soon as a villus begins to become of less height, the reverse of the process which takes place in the growth of late villi, it often happens that a crypt starts to develop very near it. Perhaps the growth of this crypt downward may have some influence on the disappearance of the villus, but crypts do not grow down near *every* villus which is beginning to disappear (Fig. 82).

A few of the reasons for connecting the disappearance of villi from the large intestine with the increase in extent of intestinal surface are:

1. The rapid growth of the intestine; the lack of growth of the villi; and the same size of the glands afterwards as before.

2. The glands and villi are independent structures; the glands develop as downgrowths, the villi as upgrowths.

3. Villi of gradually less height are formed as the surface of the intestine increases in extent and in many cases villi may disappear where no glands are near, or a gland or glands on only a small part of the villus base; some of these glands may start in the base of a villus after it is reduced to a small projection (Fig. 27).

The erroneous idea that villi disappear by growing together is very easy to arrive at because in later stages the crypts of the large intestine become so numerous that in sections there is much the appearance of numerous short villi, which are, of course, small portions of mucosa between crypts.[5]

[5] In the lower large intestine of a white rat of four days after birth, there sometimes occur, besides crypts, gutters which on surface views seem to connect the crypts with each other, but on more careful examination it is found that these gut-

Summary.

1. Crypts of Lieberkühn in the white rat develop as simple downgrowths of epithelium without any relation to the villi.

2. Crypts begin to develop after the villi are formed and make their appearance first in the rectum.

3. Villi of the large intestine slowly decrease in size and disappear as the area of the intestine increases. The rectum is found to be without villi first, next the cæcum and last the upper large intestine.

Some General Conclusions.

As with other organs, folds and villi in all forms present individual variations, but although great variation is encountered with all species, it is especially noticeable in the lower forms; to take specific examples, the folds and villi of Amia or the folds of the toad vary more among themselves than the villi of calf or cat.

Another point observed upon other organs is the recurrence of similar structures in widely differing groups, as illustrated by Amia and Bufo. These have very similar conditions of arrangement of the folds. Other examples would be the similarity between the folds of the blacksnake and those of some birds; and the similar folds of catfish and some Amphibia. These widely separated forms which have similar structures may have come to such conditions, either by similarity of environment, that is character of the food; or these types may simply indicate that all forms develop similarly and that several widely differing forms may have developed faster and reached a more specialized condition than their near relatives; or that other forms were for several causes retarded in development, and so approximated the less advanced conditions of less specialized animals.

The largest villi were usually found in the larger animals, especially when the species were nearly related. When two or more adult animals of the same species were examined, it was found that the larger animals in most cases had larger villi than the smaller ones, and when young and old animals were compared it was found that these differences were much more striking.

ters, which usually run transversely, are grooves which connect simply the mouths of glands. These occur in the rectum, and in sections the appearance is as if we had crypts with villi overhead and all gradations of villi uniting with crypts and so disappearing. This appearance is easily explained after the study of the surface of the intestine. These depressions are of late origin and are only found long after villi have disappeared.

A typical form of villus is found in the flesh-eating animals. The villi are rather long, thick, cylindrical or finger-shaped, such as found in cat, dog, lion, etc. With insectivorous mammals, this form is slightly modified; the villi may have sharper tips. The villi of insectivorous birds are similar to those of corresponding mammals, but they differ from them in being more flattened. With Raptores, the villi, although more or less flattened, approach the cylindrical or columnar type.

In the vegetable-eating mammals, and some birds past the fold stage, three general types of villi may be recognized:

1. The leaf-like or thin, broad, tongue-shaped form.
2. The long, slender, cylindrical or thread-like form.
3. The short, thick, columnar or wart-like form.

The first sort is the most common and has already been described with some modifications in rabbit, mouse, muskrat and monkey. Also in some birds.

The second or thread-like sort of villus is found in the ileum of some rodents, such as rabbit. This type is found, for example, in the intestines of cow, camel and sea-cow.

The third or thick, columnar to low wart-like forms are found in the cæca and large intestines of some grain-eating birds, as chicken, turkey, partridge, and is also found in the small intestine of horse. These villi differ from the carnivorous type because of their proportionately broader bases, less height, and fewer numbers.

With omnivora, as a usual thing, villi in mammals correspond with either the carnivorous or the herbivorous type; for instance, the raccoon has the carnivorous type and the opossum has the herbivorous type of villus. Seldon do omnivora combine both types in the same animal; however, in man such a condition may be said to exist; that is, there are leaf-like villi in the upper intestine or duodenum and columnar in the ileum.

The development of the first villi in chick very interestingly shows a number of the stages of folds which were found in the adult intestines of lower forms, as well as the conditions existing in a number of adult birds. The much later development of villi in the cæca and large intestine does not show all the fold stages which were found in the small intestine. If these stages were ever developed, there is very little indication of them at present.

The first development of villi in mammals is from straight, parallel folds, no zigzag folds are formed like those in chick. It may be that the zigzag folds were never developed, but it seems at least possible that this zigzag fold stage was once formed, but now entirely omitted, be-

cause villi in mammals are well formed at a comparatively early stage in the embryo.

Brief Summary.

1. Simple folds, villi and valvulæ conniventes involve the mucosa alone.

2. Simple mucosal folds and villi of the intestine are homologous; villi are the more specialized of these and usually occur in higher vertebrates, as mammals and birds.

3. True villi are found in a number of lower forms, although folds of different types are the usual elevations of the mucosa in all classes except birds and mammals.

4. The individual variation in shape, size and number of folds, and villi is marked in all groups, but is less characteristic of mammals.

5. Although a number of divisions of the shape of folds or villi may be made, there are intermediate conditions which connect the different divisions with each other.

6. Four general types of folds are:

   1. Long, straight, parallel.
   2. Wavy, parallel folds.
   3. Zigzag parallel folds.
   4. Net-arranged folds.

7. Four general forms of villi are:

   1. Thin, leaf-like.
   2. Thread-like or long, cylindrical.
   3. Cylindrical or finger-shaped.
   4. Low columnar or wart-like.

8. The largest villi are usually found in the largest animals.

9. The number of villi per square millimeter in many cases is largely determined by the size of the villi.

10. Carnivorous mammals usually have finger-like or cylindrical villi. Herbivora, leaf-like, thread-like or mound-like shapes. Omnivora have either the carnivorous or herbivorous type of villus or both types in the same intestine.

11. By an examination of many species of vertebrates, is is found that the following, in general, represent the steps of specialization:

   1. Few longitudinal, straight folds beginning near the pyloric valve.
   2. Numerous straight, longitudinal folds, more extensive.
   3. Slightly wavy folds throughout the intestine.
   4. Very wavy folds, numerous and thickly placed.

5. Zigzag folds (or net arranged folds).

6. Zigzag arranged villi or otherwise regularly arranged villi; and closely after this:

7. Irregularly arranged villi throughout the intestine.

8. Villi in the small intestine and cæcum, not in the large intestine.

9. Villi in the small intestine alone.

10. Valvulæ conniventes formed.

12. By embryological study, villi are found to develop from folds in the beginning, but later villi may be formed without passing through the fold stage.

13. In chicken embryos straight folds are formed first near the pylorus, these become longer, more numerous and wavy, then zigzag, and then break up into villi at the angles of the folds downwards; later villi lose their zigzag arrangement and others develop without passing through a fold stage.

14. In the white rat the early development of villi is very rapid. In the beginning longitudinal folds appear first in the duodenum, later in other parts of the small intestine. These folds break up into villi and villi are afterward formed as simple upgrowths of epithelium.

15. A study of different species of vertebrates which have folds and villi at the same time in the intestine of the adult, shows two ways in which villi are formed from folds: first, from zigzag folds, the usual way; second, from net-arranged folds.

16. Valvulæ conniventes, apparently found only in man, develop from simple, semicircular thickenings of the mucosa long after the villi are developed. They are simple, secondary mucosal elevations and bear villi on their surface.

17. At one time during the development of the intestines of mammals, villi are found throughout the large intestine including the cæcum and appendix. As the intestine grows in size and extent the villi disappear. The disappearance of the villi seems to be for the most part independent of the development of the intestinal glands or crypts of Lieberkühn.

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PLATE I.

The following plate is for the purpose of showing some of the types of folds in the lower vertebrates.

The folds are shown as they look when viewed from above after the intestine is cut open longitudinally and spread out flat.

Fig. 1. Folds from turtle. × 5 diameters.
Fig. 2. Folds from Amphiuma. × 5 diameters.
Fig. 3. Folds from the salamander Gyrinophilus. × 13 diameters.
Fig. 4. Folds from a half-grown Necturus. × 5 diameters.
Fig. 5. Folds from Catostomus. × 11 diameters.
Fig. 6. Folds from alligator. × 11 diameters.
Fig. 7. Folds from perch. × 10 diameters.
Fig. 8. Folds from blacksnake. × 5 diameters.
Fig. 9. Folds from toad. × 12 diameters.
Fig. 10. Folds from Catostomus. × 24 diameters.

PLATE I.

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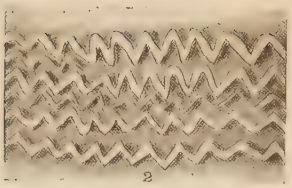

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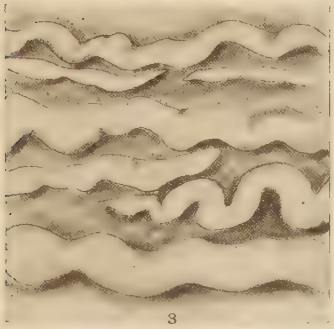

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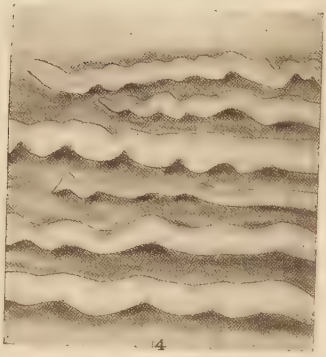

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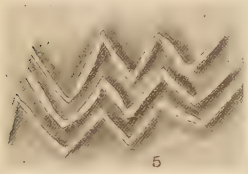

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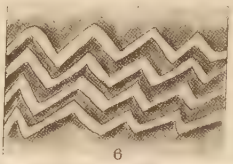

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PLATE II.

The general forms of villi found in mammalia are given in this plate. With the animals in which villi differ greatly in size or form in the different parts of the same intestine, a number of villi are figured.

All figures × 25 diameters.

Fig. 11. Villus of calf near middle of intestine (cylindrical).

Fig. 12. Villus of calf near cæcum (cylindrical).

Fig. 13. Villus of calf near pylorus (cylindrical).

Figs. 14 and 15. Front and side views from villus of muskrat near the pylorus.

Fig. 16. Villus near the cæcum of muskrat's small intestine.

Fig. 17. Villus from middle of cat's intestine (cylindrical).

Fig. 18. Villus from pyloric part of cat's intestine (cylindrical).

Fig. 19. Villus from near cæcum of cat's intestine (cylindrical).

Fig. 20. Villus or fold at pylorus of rabbit's intestine.

Fig. 21. Villus 10 cm. from pylorus of rabbit's intestine.

Fig. 22. Villus 110 cm. from pylorus of rabbit's intestine.

Fig. 23. Villus 190 cm. from pylorus of rabbit's intestine.

Fig. 24. Villus 250 cm. from pylorus of rabbit's intestine, or just above the cæcum.

Fig. 25. Villus Homo at term upper intestine.

Fig. 26. Villus Homo at term upper intestine.

Fig. 27. Villus Homo at term lower intestine.

Fig. 28. Villus Homo at term lower intestine.

Fig. 29. Vilus from bat near pylorus.

Fig. 30. Villus from bat 5 cm. from the pylorus.

Fig. 31. Villus from bat 11 cm. from the pylorus or end of villi.

Fig. 32. Villus from shrew, middle of intestine (cylindrical).

Fig. 33. Shrew, near middle of intestine (cylindrical).

Fig. 34. Villus from mouse 2 cm. from pylorus.

Fig. 35. Villus from mouse 9½ cm. from pylorus.

Fig. 36. Villus from mouse 11 cm. from pylorus.

Fig. 37. Villus from mouse 13 cm. from pylorus.

Fig. 38. Villus from mouse 18 cm. from pylorus.

Fig. 39. Villus from mouse 30 cm. from pylorus or above cæcum.

Fig. 40. Villus from the intestine of horse.

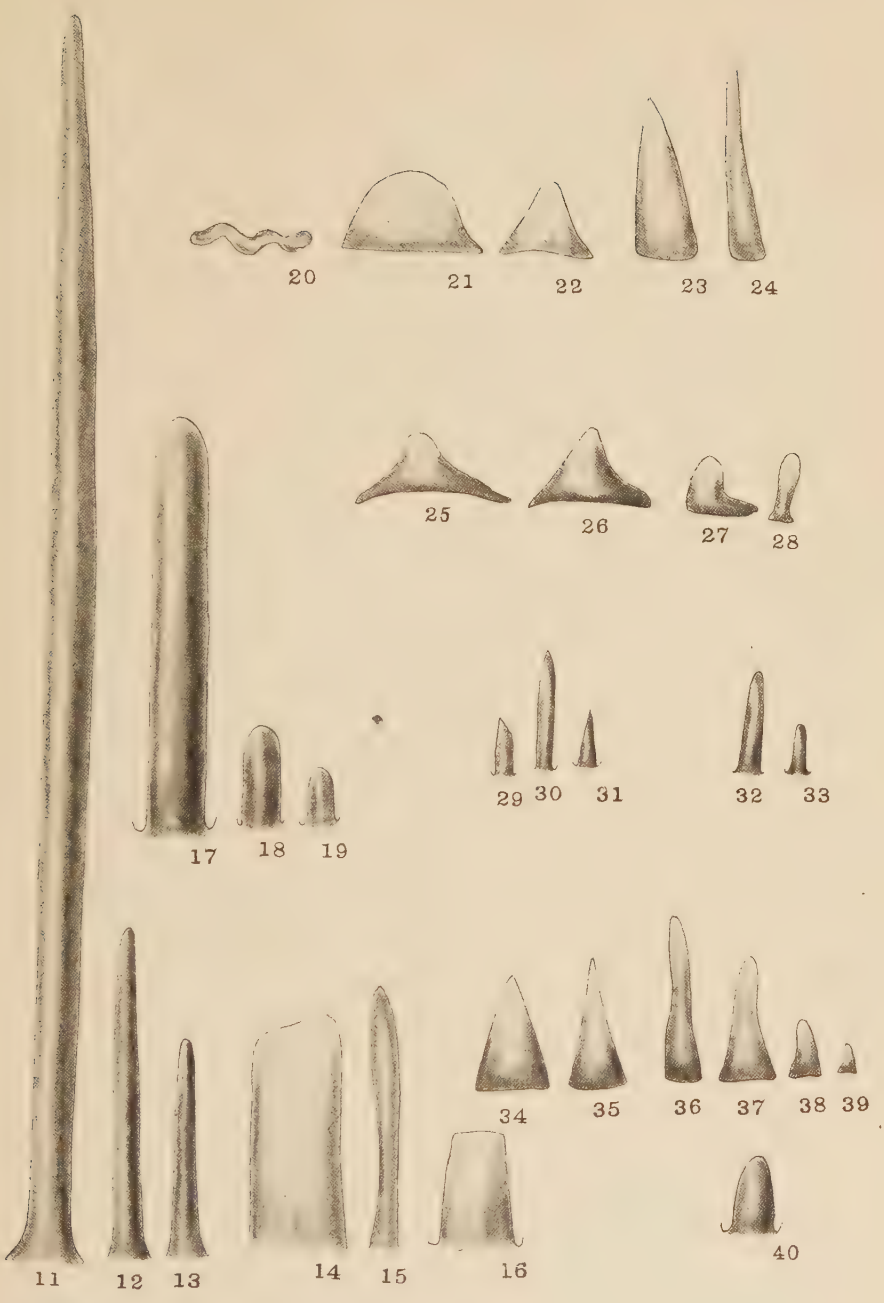
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PLATE III.

Section and surface view drawings from folds and villi of mammals and birds.

Fig. 41. Section across a spiral fold of rabbit's cæcum at time of birth. V = villi, × 50 diameters.

Fig. 42. Section across a developing valvulæ conniventes from a child at term. V=villi, × 50 diameters.

Fig. 43. Villus near pylorus of a domestic duck. × 38 diameters.

Fig. 44. (a) Arrangement of villi 110 cm. from the pylorus of a domestic duck. (b) Villus 110 cm. from the pylorus of a domestic duck. × 38 diameters.

Fig. 45. Villus from the cæcum of a domestic duck. × 38 diameters.

Fig. 46. (a) The arrangement of villi from the large intestine of a domestic duck. (b) Villus from the large intestine of a domestic duck. × 38 diameters.

Fig. 47. Section of the intestine of an eight-day chick, taken near the pylorus. × 88 diameters.

Fig. 48. Section from the intestine of an eight-day chick some distance from the pyloric valve. × 88 diameters.

Fig. 49. (a) Longitudinal section of a single fold from near the pylorus of a nine-day chick's small intestine. × 88 diameters. (b) Transsection from the intestine of the same chick a short distance from the pyloric valve. × 88 diameters.

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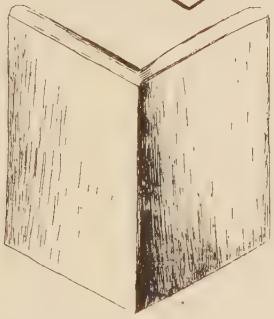

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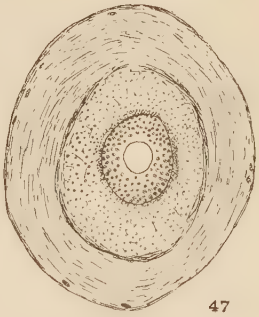

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PLATE IV.

Drawings from sections of embryo chick's intestines.

Fig. 50. (a) Transection of the small intestine of an 11-day chick. × 60 diameters. (b) Longitudinal section through folds from the duodenum of an 11-day chick. × 60 diameters.

Fig. 51. Transection of the small intestine of a 13-day chick. × 60 diameters.

Fig. 52. Longitudinal section through a single fold of a 13-day chick's intestine. × 60 diameters.

Fig. 53. Longitudinal section of the small intestine of a 14-day chick where villi are partly formed. × 60 diameters.

Fig. 54. Longitudinal section of a single fold from a 14-day chick. The larger part of the fold is where the section has cut deepest into the base, and the smaller end is where the top of the fold is cut through at the place where villi are beginning to be formed. × 60 diameters.

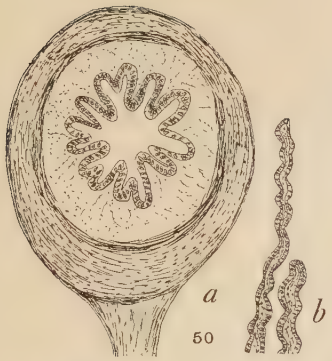
Fig. 55. Longitudinal section of the cæcum of a 13-day chick. × 60 diameters.

Fig. 56. Villi from the cæcum of a 16-day chick. × 60 diameters.

Fig. 57. Villus bud from the small intestine of a 3-5-day white rat. × 300 diameters.

Fig. 58. Section of large intestine of a 14-day chick. × 270 diameters.

Fig. 59. Epithelial projection or villus bud from the large intestine of an embryo white rat. × 417 diameters.



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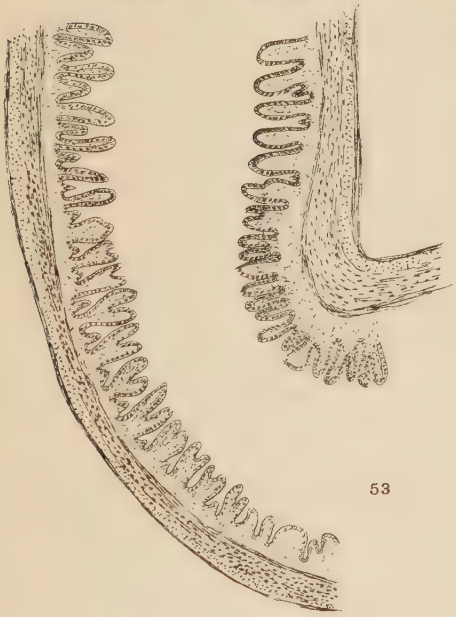

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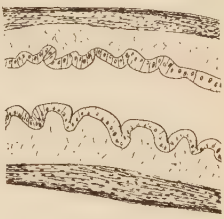

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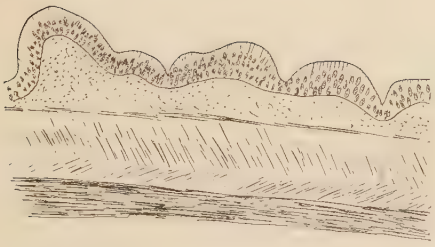

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PLATE V.

Figures of wax reconstructions from the intestine of chick embryos.

Figs. 60 and 61. Folds from 8-day chick. Epithelium alone shown (near the pyloric valve). × 100 diameters.

Fig. 62. Part of intestine from 9-day chick (near pyloric valve). ×50 diameters.

Fig. 63. Part of intestine of 11-day chick, looking almost directly down on folds. × 50 diameters.

Fig. 64. Reconstruction of single fold of 11-day chick. × 100 diameters.

Fig. 65. Reconstruction of intestine of a 14-day chick's large intestine. × 50 diameters.

Fig. 66. Reconstruction in wax from the cæcum of a 14-day chick when villi are quite well formed. × 50 diameters.

Fig. 67. Wax reconstruction from cæcum of 13-day chick. × 50 diameters.

Fig. 68. Part of intestine from 13-day chick. Folds quite wavy. × 50 diameters.

Fig. 69. Small 14-day chick single fold near the pylorus. × 100 diameters.

Fig. 70. Reconstructions in wax of a single fold near the pyloric valve from the intestine of an advanced 14-day chick. The fold has begun to break into villi at the fold angles. × 100 diameters.

PLATE V.

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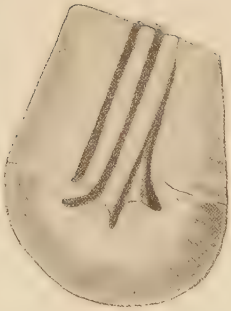

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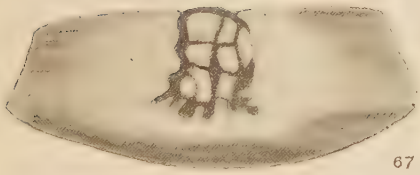

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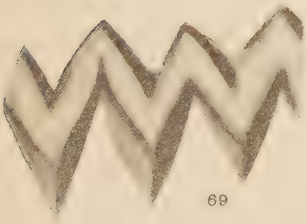

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PLATE VI.

Figures of sections and wax reconstructions from the intestine of embryo white rats, to show the development of folds and villi.

Fig. 71. Cross section of white rat's intestine; length of embryo 3.3 cm. × 56 diameters.

Fig 72. Same as Fig. 61 near the pylorus. × 56 diameters.

Fig. 73. Section of intestine from white rat of 3.4 cm. Villi partly formed. × 56 diameters.

Figs. 74 and 75. Sections of different stages from a white rat of 2.3 cm. in length. × 56 diameters.

Fig. 76. Reconstruction of a single fold removed from near the pylorus of a young embryo of white rat. Thick end of fold is taken nearest the pylorus. × 100 diameters.

Fig. 77. Reconstruction of the rest of the intestine from which the above was taken. The pyloric end of the piece is away from the observer and has one more fold than the end towards the observer. × 100 diameters.

Fig. 78. Portion of white rat's intestine after the folds are beginning to break up into smaller parts. × 133 diameters.

Figs. 79 and 80. Different views of reconstructions showing folds largely divided into villi. × 100 diameters.

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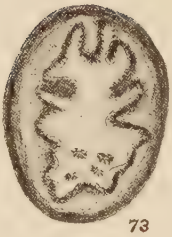

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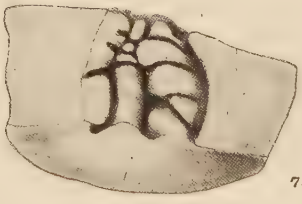

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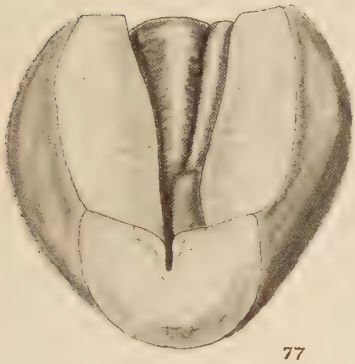

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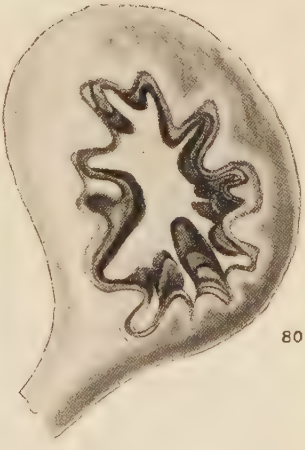

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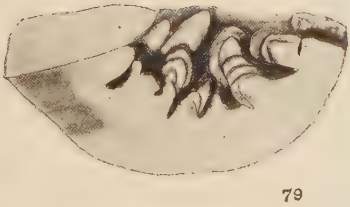

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PLATE VII.

Figures illustrating the development of the crypts of Lieberkühn and the disappearance of villi from the large intestine of young white rats.

Fig. 81. Surface views of villi and crypts from the small intestine of a 3-day white rat. V=villus, c=crypt. × 50 diameters.

Fig. 82. Sections from the large intestines of several white rats to show the disappearance of villi. All the figures × 58 diameters.

(a) Five days after birth.
(b) Six days after birth.
(c) Eight days after birth.
(d) Eight days after birth, more advanced stage.
(e) Eleven days after birth.

Fig. 83. Villi and beginning crypts from a 3-5-day white rat (after birth). C=crypts. × 300 diameters.

Figs. 84 and 85. Beginning crypts from the small intestine of a white rat 3-4 days after birth. × 300 diameters.

Fig. 86. Crypt of Lieberkühn from the intestine of a 4-day white rat. × 300 diameters.

Fig. 87. Lieberkühn crypt from the small intestine of a white rat, 36 days after birth. × 300 diameters. V = parts of villi, c = crypt and s = surface of the intestine between villi.

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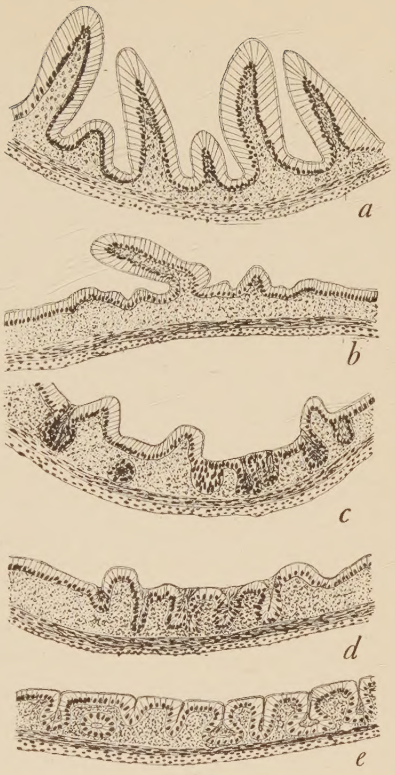

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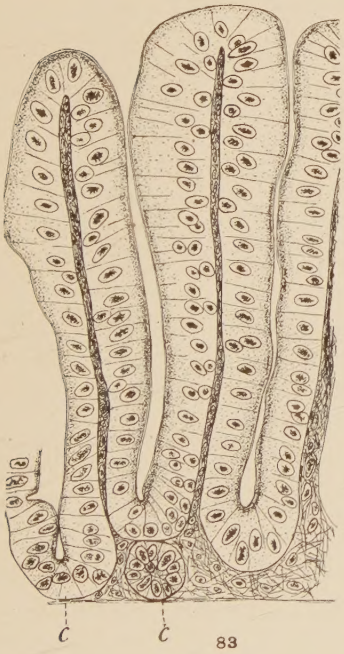

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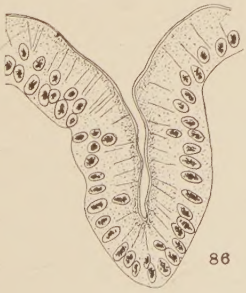

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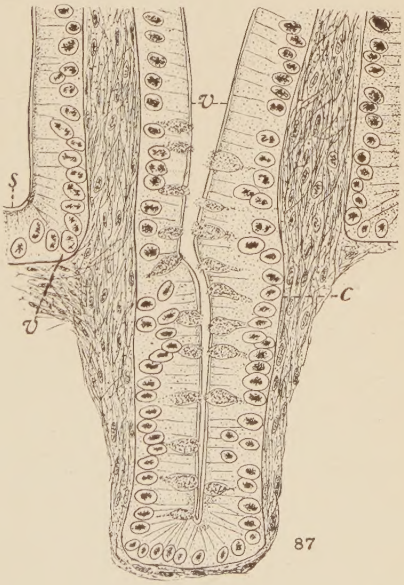

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